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Veterinary Vaccinology

edited by

P.-P. Pastoret
Université de Liège,
Department of Immunology-Vaccinology,
Faculty of Veterinary Medicine,
Sart-Tilman
Liège, Belgium

J. Blancou
Office International des Epizooties,
Paris, France

P. Vannier
CNEVA
Ploufragan, France

C. Verschueren
FEDESA/COMISA
Brussels, Belgium

ELSEVIER
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TABLE 4

Peptide vaccines for Parvo virus

	Antiviral activity*			Protection in target animals**		
	ELISA	NT	T cell	Single dose	Double dose	Control
Langeveld et al. (1994)	+	+/–	–	1/1	9/9	0/4
Langeveld et al. (in prep.)	+	–	nt	1/6	nt	0/6

*nt = Not tested; + = activity present; – = no activity; +/– = activity in some individual animals.
**Ratio = number of protected animals/number of total animals.

which is shown to be highly conserved between strains and types, a peptide has been defined which readily induces full protection against disease in dogs after CPV infection using two vaccinations. Mink were protected with the same peptide vaccine against another parvovirus (mink enteritis virus) after a single vaccination. This appears to be the first example of a peptide vaccine which seems as effective as the classical vaccine based on whole virus.

9.5. CONCLUSION

From this, we speculate that it will be possible to develop effective peptide vaccine against other DNA viruses, notably those depending on humoral immunity for protection.

We further speculate that full protective peptide vaccines as effective as classical ones, are feasible in case of RNA viruses, like FMDV, if, in addition to the loop-peptide a peptide can be defined and constructed which represents one of the additional discrete neutralizing antigenic sites of FMDV.

PART 10. OTHER TYPES OF VACCINES (i.e., WITH CYTOKINES)

W. Strube

The immune response can be divided into two functional groups: the innate or primitive immune system and the adaptive immune system (Büttner, 1993). The innate immune system, which represents the first barrier in the combat against infectious diseases, is mediated by antigen non-specific actions of neutrophils, natural killer cells, macrophages and by soluble factors like the complement system. The adaptive immune system is represented by the antigen-specific B- and T-cells. Both parts of the immune response are modulated by, and interact through, cytokines, including interleukins (IL), interferons (IFN), colony stimulating factors (GSF) and tumour necrosis factors (TNF) (Roitt et al., 1989). IL 1 is synthesized by antigen-presenting cells and contribute to T- and B-cell stimulation (Mizel, 1982). IL-2, IL-4, IL-5, and IFN-gamma are involved in clonal proliferation and differentiation of immune cells (Kelso, 1989; O'Garra et al., 1988) IL-2 contributes especially to proliferation, differentiation and cytotoxic activity of T-cells (Farrar et al., 1982). IFN-gamma stimulates macrophages and induces expression of MHC class II (Roitt et al., 1989). Due to their physiological function in the immune system cytokines,

when combined or applied simultaneously with immunog ems, may influence immunogenicity of vaccines. Therefore, cytokines were evalua ed as 'natural' adjuvants in various vaccine models. Schijns and co-workers comp red different cytokines in a rabies challenge model in mice (Schijns et al., 1994). Whereas TNF-alpha and IL-1-alpha, when applied shortly before rabies vaccinatic n only marginally induced protection against challenge infection, IFN-gamma an . multiple applications of IL-2, respectively, markedly increased immunogenicity f llowing vaccination. Combined administration of IFN-gamma and IL-2 synergisi cally enhanced formation of neutralizing antibodies following rabies vaccination b it did not further increase resistance to challenge. Reddy and colleagues report ed that administration of recombinant bovine IL-1β in combination with a BHV . live attenuated vaccine increased the vaccine induced cytotoxic immune respc ase in cattle and reduced challenge virus replication following experimental infe tion (Reddy et al., 1990). The same team also tested recombinant bovine IL-2 as . n adjuvant of a live BHV1 vaccine (Reddy et al., 1989). Five consecutive applica ions of IL-2 significantly enhanced humoral and cellular immune responses as well as clinical protection following immunization with a live attenuated BHV1 va ccine in cattle. No additive effect was observed when IL-1 and IL-2 were administ red together (Reddy et al., 1993). Hughes and co-workers confirmed the efficacy o IL-2 in cattle and demonstrated that multiple injections of IL-2 following vaccina ion with a BHV1 glycoprotein gD vaccine significantly increased BHV1 specific · ytotoxicity and gD specific lymphocyte proliferation response compared to vaccina ted animals that were not treated with IL-2 (Hughes et al., 1991). In the ovine syster , IL-1 and 2, as well as TNF, have been produced by recombinant DNA techniques (lash et al., 1993). Adjuvant studies using avidin as a model antigen demonstrated hat ovine IL-1 significantly increased antibody formation in sheep (Andrews et al., 1 94). The use of cytokines as natural adjuvants may even allow the stimulation of spe ific immunoglobulin classes. The use of a recombinant vaccinia virus expressing m rine IL-5 and influenza HA protein demonstrated that IL-5 selectively enhanced muc sal IgA response specific for HA in mice (Ramsay and Kohonen-Corish, 1993). In summary, all these results indicated that cytokines may indeed be used to improve fficacy of vaccines. Babiuk's group has already constructed a molecular chimera c a *Pasteurella haemolytica* leukotoxin and IL-2 (Hughes et al., 1992). Because of s ufety, efficacy and manufacturing aspects, such antigen–cytokine complexes may epresent future vaccines.

PART 11. FUTURE TYPES OF VA CCINATION

R.H. Meloen

This section deals with most of the veterinary vaccines we may expect in the future. Presently, two sorts are emerging: one that deals wit vaccines against 'self' protein, notably hormones. These vaccines will be dealt w ith elsewhere. The other one deals with DNA vaccination.

11.1. DNA VACCINATION

DNA plasmids can be used for DNA vaccination (D avis et al., 1993; Robinson et al., 1993) and have a number of appealing advantage : large proteins can be easily expressed in eukaryotic cells, vaccine design is relati ely easy, the vaccine itself is